ACTION DUE Reply
DUE DATE 1.27.05
INITIALS mh

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	27 OCT 2004
Applicant's or agent's file reference 00786/443WO1	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/20893	30 June 2004 (30.06.2004)	14 July 2003 (14.07.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/44, 31/435 and US Cl.: 514/277, 344, 345, 356, 357

Applicant

THE GENERAL HOSPITAL CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/20893

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-17	YES
	Claims NONE	NO
Inventive step (IS)	Claims 1-17	YES
	Claims NONE	NO
Industrial applicability (IA)	Claims 1-17	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-17 meet the criteria under PCT Article 33(2) for novelty because the references fail to teach the presently claimed composition comprising the claim specified pyridine compounds or methods for treating or preventing a vascular disease; determining whether a candidate gene is a component of or affects a molecular pathway involved in vasculogenesis; identifying a gene in a molecular pathway involved in vasculogenesis; or identifying a component of a molecular pathway involved in vasculogenesis.

Claims 1-17 meet the criteria under PCT Article 33(3) for inventive step because the references fail to teach or suggest the presently claimed composition comprising the claim specified pyridine compounds or methods for treating or preventing a vascular disease; determining whether a candidate gene is a component of or affects a molecular pathway involved in vasculogenesis; identifying a gene in a molecular pathway involved in vasculogenesis; or identifying a component of a molecular pathway involved in vasculogenesis.

Claims 1-17 meet the criteria under PCT Article 33(4) because the presently claimed composition comprising the claim specified pyridine compounds or methods for treating or preventing a vascular disease; determining whether a candidate gene is a component of or affects a molecular pathway involved in vasculogenesis; identifying a gene in a molecular pathway involved in vasculogenesis; or identifying a component of a molecular pathway involved in vasculogenesis would have applicability in the medical industry.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-9 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: the description is enabling for a method of treating a vascular disease, but not for preventing a vascular disease.

The burden of enabling the prevention of a disease such as a vascular disease would be much greater than that of enabling the treatment of a disease such as a vascular disease. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing a vascular disease or how a patient could be kept from every being susceptible to this disease. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agents for preventing a vascular disease.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified active could actually prevent a vascular disease by simply administering, by any method, an amount of the claim specified active agents. The specification fails to enable one of ordinary skill in the art to practice the prevention of a vascular disease.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of absolute success. Since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex/poorly understood as a vascular disease, the specification, which lacks an objective showing that a vascular disease can actually be prevented, is viewed as lacking an adequate written description of the same..